

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 45, line 2 with the following amended paragraph.

Several mutations in APP associated with early onset Alzheimer's disease have been shown to alter A β peptide processing. These flank the N- and C-terminal cleavage sites that release [[A□]] A β from APP. These cleavage sites are referred to as the β -secretase and γ -secretase cleavage sites, respectively. Cleavage of APP at the β -secretase site creates a C-terminal fragment of APP containing 99 amino acids of 11,145 daltons molecular weight. The Swedish KM NL mutation immediately upstream of the β -secretase cleavage site causes a general increase in production of both the 1-40 and 1-42 amino acid forms of [[A□]] A β peptide. The London VF mutation (V717 F in the APP770 isoform) has little effect on total [[A□]] A β peptide production, but appears to preferentially increase the percentage of the longer 1-42 amino acid form of [[A□]] A β peptide by affecting the choice of β -secretase cleavage site used during APP processing. Thus, we sought to determine if these mutations altered the amount and type of [[A□]] A β peptide produced by cultured cells cotransfected with a construct directing expression of Hu-Asp2.

Please replace the substitute sequence listing (pages 1-43) filed on March 26, 2001 with the second substitute sequence listing (pages 1-41) submitted herewith.